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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,159	05/28/2003	Sean Farmer	19374-501	1649

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,159	FARMER ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-24,34-43 and 49-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-24,34-43 and 49-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group 3 (claims 14-24, 34-43 and 49-69) in the reply filed on 4/29/2005 is acknowledged.

Claims 14-24, 34-43 and 49-69 are pending and under examination.

Claim Rejections - 35 USC § 112

Claims 14-24, 34-43 and 49-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The as-filed specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Nature of instant invention is directed to the use of topical compositions with probiotics to control microbial infections.

The breadth of the claims is directed to a method for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections by applying topically to skin or mucous membrane probiotic composition with *Bacillus* species. Some claims are further drawn to generic representatives assigned to various species of *Bacillus coagulans, Bacillus subtillus, Bacillus laterosporus* and *Bacillus laevolacticus*. Some claims are further drawn to bacterial, yeast, fungal and/or viral infections including vaginal infections including *Staphylococcus*, *Tichophyton* and *Candida* species.

The as-filed specification only discloses various topical compositions with *Bacillus* cells as intended to control microbial infections and the specification suggests some generic doses and/or generic protocols of administration for unidentified generic patients.

As related to the actual methods for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections the specification only discloses the ***in vitro*** assays (example 1, pages 24-27) of antimicrobial activity **of one** representative of *Bacillus coagulans* ATCC 31284 (page 12, line 7) towards infections limited to *Tichophyton* species and *Candida* species. The protocol of *in vitro* assays is based on measuring inhibition zones on agar plates. No animal cells including skin or mucous membrane cells are involved in the *in vitro* assays. No animals were used as *in vivo* model systems for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections.

Thus, the specification does not adequately teach how to effectively inhibit bacterial, yeast, fungal and/or viral infections including vaginal infections because no animal cells or live

animals were used. Therefore, the specification does not and cannot adequately teach how to effectively treat bacterial, yeast, fungal and/or viral infections including vaginal infections because no animal cells and/or no live animals were used to demonstrate inhibition of infections by probiotic compositions with *Bacillus*. Further, the burden of enabling the prevention of a disease (ie. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those animals including humans susceptible to any and all claimed infections and/or diseases and the difficulty of proof that the administration of the drug with probiotic *Bacillus* was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to any and all claimed bacterial, yeast, fungal and/or viral infection including vaginal infections within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed compounds in preventing these infections. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

With regard to unpredictability of the claimed method(s) as drawn to a generic *Bacillus* it should be noted that there are pathogenic *Bacillus* species that could qualify as probiotics by virtue being alive and competitive (invasive) but would inhibit, if not kill, animal cells and animal models.

With regard to unpredictability of the claimed method(s) as drawn to generic representatives assigned to various species of *Bacillus coagulans, Bacillus subtillus, Bacillus laterosporus* and *Bacillus laevolacticus*, it is noted that only one and specific strain ATCC 32184

has been used in the in vitro assays on agar plates as disclosed in the as-fled specification. However, not only various species are different in their manifestation of antimicrobial activity but also even representatives of one species do not inhibit all claimed bacterial, yeast, fungal and/or viral infection including vaginal infections within the scope of the presently claimed invention. For example: the reference by Sytnik (IDS reference; Mikrobiologicheski Zhurnal, 1989, 51, 1:82-87) demonstrates that at least some strain(s) of the claimed *Bacillus coagulans* do not inhibit all clinical *Staphylococcus* infections (see table 3).

With regard to unpredictability of the claimed method(s) as drawn to inhibiting various topical and mucous membrane infections including vaginal infection, Seligman (British Journal of Obstetrics and Gynaecology. October, 1995. Vol. 102, pages 763-764) teaches that the studies of the use of probiotics or of bacilli in the treatment of vaginitis have almost all been limited, uncontrolled and have given variable results (page 763, col. 2, par. 4, lines 1-4). Thus, the state of the art provides no reasonable expectation of success.

Seligman also teaches that the ability of bacteria to adhere to animal epithelial cells is an important factor in colonization of mucous membrane or vagina and that the different species show varying effects (page 763, col. 2, par. 2. lines 1-4). The instant specification does not demonstrate that the claimed *Bacillus* species including only one exemplified ATCC 31284 (that has antimicrobial activity towards *Tichophyton* species and *Candida* species) are capable to adhere to the animal epithelial cells and/or to colonize the animal epithelial cells in competitive exclusion or in interactions with other microbes or infectious agents. Thus, the ability of the claimed *Bacillus* species including one exemplified ATCC 31284 to adhere to animal cells

including mucous membrane cells is unpredictable and, therefore, the selection of desirable *Bacillus* species requires undue experimentation.

The claimed doses and/or protocols of administration are generic considerations and they are not supported for the whole breath of instant claims because neither claimed doses nor claimed protocols have been demonstrated in models involving animal cells and/or live animals and because the claimed doses have not been demonstrate as effective for colonization of skin or mucous membrane including vagina. The specification does not teach how to extrapolate data obtained from *in vitro* antimicrobial studies on agar plates as obtained with one strain towards a limited number of infections to the development of effective *in vivo* mammalian including human therapeutic treatment, in order to commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan might predict the efficacy of methods for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections by applying topically to skin or mucous membrane probiotic composition with *Bacillus* species. As such, the invention must be considered unpredictable. Thus, in the absence of working examples or detailed guidance in the specification, the intended uses for composition comprising probiotics *Bacillus* species are fraught with uncertainties. Without sufficient guidance the methods as claimed are unpredictable and the experimentation left to those skilled in the art is unnecessarily, improperly, extensive and undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16, 24, 34-39, 49-50, 55-57, 65-67 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,871,539 (Hata et al.).

Claims are directed to a method for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections wherein the method comprises step of applying topically to skin or mucous membrane probiotic composition with *Bacillus* species. Some claims are further drawn to generic representatives assigned to various species of *Bacillus coagulans, Bacillus subtillus*. Some claims are further drawn to forms of the compositions including liquid and solid.

US 4,871,539 discloses a method of using probiotic composition with *Bacillus* species (example 5 including col. 18, lines 34-37 and tables 4-6) wherein the method comprises step of applying topically to skin or mucous membrane (col. 8, line 52) live bacterial cells (col. 9, line38) of *Bacillus* species A and B that are *Bacillus coagulans* strain 2930 and *Bacillus subtilis* strain 3335 (table 3). Protocol is twice a day for 4 days (col.18, lines 34-37). Topical applications include pubic and vaginal areas (col. 11, lines 1-2 and line 28). Forms of the compositions are liquids (col. 10, lines 3-5) and suppositories (col. 11, line 21). The liquid solutions include sugars. The cited patent teaches that addition of *Bacillus* resulted in extended periods of beneficial effects (col. 22, line 48) particularly when pathogens were present in the vaginal area (col. 11, lines 3-7).

Thus, the prior art method comprises the same active step and structural elements as the claimed methods. When a claim recites using an old composition or structure and the use is

directed to a result or property of that composition or structure then the claim is anticipated. See MPEP 2112.02.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-16, 20-22, 24, 34-39, 41-43, 49-50, 55-57, 59-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,871,539 (Hata et al.) taken with Gibson et al. (Gastroenterology. 1995. 108: page 975) and JP 3-192200

Claims 14-16, 24, 34-39, 49-50, 55-57, 65-67 as explained above. Claims 20-22, 41-43 are further drawn to incorporation of FOS into probiotic compositions. Claims 59-64 are further drawn to incorporation of additional bath oils, salts, surfactants into probiotic compositions.

US 4,871,539 is relied upon as explained above. It teaches incorporation of sugars into probiotic compositions for application to mucous membranes but it is lacking disclosure about sugars such as FOS and additional bath oils, salts, surfactants. .

However, Gibson teaches that addition of FOS stimulates probiotic bacteria that come into contact with mucous membrane (abstract).

JP 3-19220 teaches addition of salts and surfactants into detergent compositions with *Bacillus coagulans* and *Bacillus subtilis* cells and/or products (English abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add the probiotic growth promoting substances including

FOS and the additional components including oils, salts, surfactants suitable for topical applications with a reasonable expectation of success in topical delivery of viable and effective probiotic compositions comprising *Bacillus* species. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

May 27, 2005

VERA AFREMOVA

PRIMARY EXAMINER